## (19) World Intellectual Property Organization International Bureau





(43) International Publication Date 31 January 2002 (31.01.2002)

PCT

## (10) International Publication Number WO 02/08213 A1

- (51) International Patent Classification?: C07D 295/185, A61K 31/495, A61P 35/00, C07K 5/062, C07F 9/09, C07D 295/088, C07C 217/74, C07D 233/61
- (21) International Application Number: PCT/GB01/02964 (22) International Filing Date:
- (25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 00401977.4

00401976.6

7 July 2000 (07.07.2000) EP

4 July 2001 (04.07.2001)

- 7 July 2000 (07.07.2000) EP
- (71) Applicant (for all designated States except US): ANGIO-GENE PHARMACEUTICALS LIMITED [GB/GB]; 14 Plowden Park, Aston Rowant, Watlington, Oxfordshire OX9 5SX (GB).
- (72) Inventor; and
- (75) Inventor/Applicant (for US only): ARNOULD, Jean, Claude [FR/FR]; Z.I. La Pompelle Boîte postale 1050. 51689 Reims Cedex 2 (FR).

- (74) Agents: BRYANT, Tracey et al.; Astrazeneca, Global Intellectual Property, Alderley Park, P.O. Box 272, Mereside, Macclesfield, Cheshire SK10 4GR (GB).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ŻW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

## Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COLCHINOL DERIVATIVES AS ANGIOGENESIS INHIBITORS

(57) Abstract: The invention related to colchinol derivatives of the formula (I): Wherein: R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are each independently hydroxy, phosphoryloxy (-OPO<sub>3</sub>H<sub>2</sub>), C<sub>1-4</sub>alkoxy or an in vivo hydrolysable ester of hydroxy, with the proviso that at least 2 of R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are C<sub>1-4</sub>alkoxy; A is -CO-, -C(O)O-, -CON(R<sup>8</sup>)- (wherein R<sup>8</sup> is hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-3</sub>alkoxyC<sub>1-3</sub>alkyl, aminoC<sub>1-3</sub>alkyl or hydroxyC<sub>1.3</sub>alkyl); a is an integer from 1 to 4 inclusive; R<sup>a</sup> and R<sup>b</sup> are independently selected from hydrogen, hydroxy and amino; B is -O-, -CO-, N(R9)CO-, -CON(R9)-, -N(R9)C(O)O-, -N(R9)CON(R10)-, -N(R9)SO<sub>2</sub>-, -SO<sub>2</sub>N(R9)- or a direct single blond (wherein  $R^9$  and  $R^{10}$  are independently selected from hydrogen,  $C_{1-3}$  alkyl,  $C_{1-3}$  alkyl, amino  $C_{1-3}$  alkyl and hydroxy  $C_{1-3}$  alkyl); b is O or an integer from 1 to 4 inclusive, (provided that when bis O, B is a single direct bond); D is carboxy, sulpho, tetrazolyl, imidazolyl, phosphoryloxy, hydroxy, amino, N- $(C_{1-4}alkyl)$ amino, N,N-di $(C_{1-3}alkyl)$ amino, or of the formula- $Y^1(CH_2)_0R^{11}$  or -NHCH(R<sup>12</sup>)COOH; [wherein Y<sup>1</sup> is a direct single bond, -O-, -C(O)-, -N(R<sup>13</sup>)C(O)- or -C(O)N(R<sup>13</sup>)- (wherein R<sup>13</sup> is hydrogen,  $C_{1-4}$ alkyl, $C_{1-3}$ alkoxy $C_{2-3}$ alkyl, amino $C_{2-3}$ alkyl or hydroxy $C_{2-3}$ alkyl); e is O or an integer from 1 to 4 inclusive.

